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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/781,117 | 02/08/2001 | Jennifer L. Hillman | PC-0034 US | 1679 |

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| EXAMINER |
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CHERNYSHEV, OLGA N

| ART UNIT | PAPER NUMBER |
|----------|--------------|
| 1646 | |

DATE MAILED: 12/17/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|------------------------------|--------------------------------|----------------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 09/781,117 | HILLMAN, JENNIFER L. |
| | Examiner Olga N. Chernyshev | Art Unit 1646 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on ____.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-20 is/are pending in the application.

4a) Of the above claim(s) 7-20 is/are withdrawn from consideration.

5) Claim(s) ____ is/are allowed.

6) Claim(s) 1-6 is/are rejected.

7) Claim(s) ____ is/are objected to.

8) Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on ____ is/are: a) accepted or b) objected to by the Examiner.

 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on ____ is: a) approved b) disapproved by the Examiner.

 If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. ____.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.

4) Interview Summary (PTO-413) Paper No(s) ____.

5) Notice of Informal Patent Application (PTO-152)

6) Other: ____.

DETAILED ACTION

Response to Amendment

1. Claims 1-20 are pending in the instant application.

Claims 7-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8.

Claims 1-6 are under examination in the instant office action.

2. The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4. Applicant's arguments filed on October 10, 2002 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 101

5. Claims 1-6 stand rejected under 35 U.S.C. 101 for reasons of record in section 4 of paper No. 10. Briefly, the instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose the biological role of this protein or its significance.

Applicant traverses the rejection on premises that "TRP is supported by a well established utility based on its structural and functional identity with TIMM8b, disclosed in the specification as a mitochondrial protein involved in neurodegenerative disorders, such as Mohr-

Tranebjaerg syndrome (page 4, last paragraph and page 5, first paragraph of the Response).

Applicant urges to pp.1-2 of the instant specification and the publication of Paschen et al., 2000 of IDS, Paper No. 3. This has not been found to be persuasive for the following reasons.

As it is clearly explained in the instant specification, pp.1-2, TRP of the instant invention is TIMM8b-related protein. It is also clear from the instant specification that what is known about TIMM8b proteins is that they resemble DDP and the yeast family of TIM mitochondrial proteins, and that “[t]he human homologue of Tim8 is encoded by the DDP1 (deafness/dystonia peptide) gene, which is associated with the Mohr-Tranebjaerg syndrome, a progressive neurodegenerative disorder leading to deafness” (Paschen et al., 2000, abstract). The instant specification fails to provide any evidence or sound scientific reasoning that would support a conclusion that TRP of the instant invention, which bears 85% of identity to TIMM8b proteins, which in turn bare homology to the proteins encoded by the gene associated with the Mohr-Tranebjaerg syndrome, would also be associated with the Mohr-Tranebjaerg syndrome or with any or all of “various neurodegenerative and neuromuscular diseases involving defects in oxidative phosphorylation” (page 4, third paragraph of the Response).

Applicant further submits that specific and substantial asserted utility of the claimed polynucleotides lies in the field of detection and quantification of “differential gene expression for diagnosis of a disorder”. Disorders associated with differential expression include cancer, particularly breast cancer, ovarian cancer, and kidney cancer” (page 6, second paragraph of the Response). Assertion of this utility is alleged to be supported by the data of Table 2 on page 39 of the instant specification. However, the data of Table 2 is not definite. It is not clear what is the difference in the degree of expression of TRP in cancer/normal tissue samples: some of the

control results, for example, for ovary tumor, seem to be absent; it is also not apparent, for example, for breast tumor and kidney tumor, how many samples were analyzed. If the results of Table 2 present the data obtained from a single sample, or less than three, for each of the cases of breast tumor, ovary tumor and kidney tumor, one of ordinary skill in the art would readily recognize that more statistical data is needed in order to make a sound scientific conclusion that TRP of the instant invention is clearly and specifically associated with these three cancers and, therefore, can be used as a marker for these diseases.

Thus, because the instant specification does not disclose a credible, specific and substantial utility for the encoded protein then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

6. Claims 1-6 stand rejected under 35 U.S.C. 112, first paragraph for the reasons of record in section 5 of Paper No. 10. Briefly, since the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.
7. Claims 2 and 6 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record in sections 7 and 8 of Paper No. 10.
8. Claim 2 is indefinite for recitation of "a fragment" of SEQ ID NO:5. Applicant submits that "SEQ ID NO: 5 aligns over 321 base pairs of its sequence with the majority of the open reading frame of SEQ ID NO: 2 and is clearly therefore a fragment of SEQ

ID NO: 2" (page 7, third paragraph of the Response). The Examiner disagrees. Regardless of the fact that a sequence can contain untranslated regions, such sequence must be described in full in order to be defined. Therefore, if a fragment of SEQ ID NO: 5 contains untranslated regions not presented in SEQ ID NO: 2, then it is a fragment of a different sequence and not of SEQ ID NO: 2.

9. Claim 6 is indefinite for recitation of "a protein", which is produced by the host cell of claim 5 and for missing a critical relationship because the claim is not limited to the host cell of claim 5 or a vector of claim 4.

Applicant's arguments that "the complementary sequence to a polynucleotide encoding an open reading can, itself, encode a protein" (page 8 of the Response) contradict fundamental knowledge in modern biology. Complementary sequences do not encode the same protein that is encoded by the coding strand of DNA. This is why the complementary strand of a DNA encoding a protein is referred to as the antisense strand. If Applicant is aware of any art, which demonstrates the opposite point of view, then Applicant is strongly encouraged to make such art of record.

Conclusion

10. No claim is allowed.

11. This application contains claims 7-20 drawn to an invention nonelected with traverse in Paper No. 8. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original

signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D. *OC*
December 13, 2002

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✓ (703) 308-0196
IP *OC* 12/13/02
JAN 2003